REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Statement of the Substance of the Interview

Applicants thank Examiner Tristan Mahyera and Examiner Michael Woodward for the courtesies extended during an interview with Applicants' representative, Yang Tang, on February 27, 2009. During the interview, the reasons a person with ordinary skill in the art would combine the references and the teaching of the references were discussed. The Examiners indicate that the rejection under 35 U.S.C. §103(a) will be reconsidered upon submission of a response to the Office Action.

II. Status of the Claims

No claim amendments are made in this response. Claims 1-31, 36-38, 40 and 44 are under examination, with claims 32-35, 39, 41-43 and 45-95 withdrawn. Upon allowance of the product claims, Applicants respectfully request that the corresponding method claims be rejoined for examination.

III. Rejection of Claims under 35 U.S.C. §103(a)

A. Reiner and Ryde

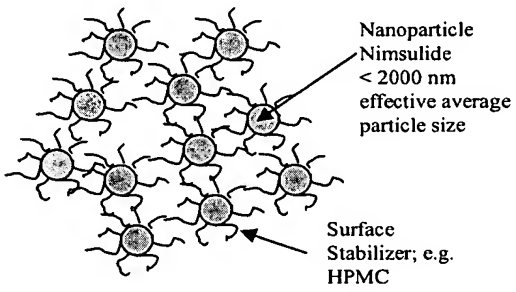
Claims 1-15 and 27-31 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over U.S. Patent No. 5,711,961 to Reiner et al. ("Reiner") in view of U.S. Patent No. 6,375,986 to Ryde et al. ("Ryde"). Applicants respectfully traverse the rejection.

(1) The teaching of Reiner

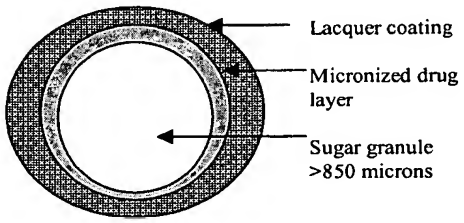
The claimed invention is directed to a nimesulide composition comprising nimesulide particles having an effective average particle size of less than 2000 nm and at least one surface stabilizer adsorbed on the surface of the nimesulide particles. In contrast, Reiner discloses a chewing gum tablet comprising a mixture of gum base and sugary microgranules, an active

ingredient adsorbed on the sugary microgranules, and a lacquer coating surrounding the core of the tablet.

For easy comparison, the claimed composition and the chewing gum tablet of Reiner are illustrated in the diagrams below:



(A) claimed composition



(B) Reiner's chewing gum

Reiner is deficient in at least the following aspects: (i) Reiner fails to teach nimesulide particles having an effective average particle size of less than 2000 nm; and (ii) Reiner fails to teach any surface stabilizer, let alone a surface stabilizer adsorbed on the surface of the nimesulide particles

Concerning point (i), the Examiner asserts that Reiner teaches a particle size of about 850 microns (Office Action, page 4, lines 6-7). In fact, Reiner teaches that the sugary microgranules have a diameter of 850 microns (column 4, line 57) but does not mention the particle size of the active agent other than to mention that it was micronized, i.e. in the micron size range. One skilled in the art would not have deduced the effective average particle size of nimesulide as claimed from a description of the size of a sugar granule or from a mention that the drug layer is micronized. Moreover, col. 4 ln. 64 through col. 5, ln. 6 of Reiner teaches that the micronized drug is suspended in a syrup and applied onto the sugar granules. The weight of the granules were taken to determine how much of "drug had actually been absorbed" onto the granule. Reiner clearly teaches absorbing drug onto a sugar granule.

In relation to point (ii), the ingredients, e.g., HPMC, polyethylene glycol, etc., of Reiner's chewing gum tablet do not read on the surface stabilizer of the claimed invention. According to the claimed invention, when the particle size is reduced to the submicron range, the particles of

the active agent tend to agglomerate to regain stability. Therefore, in the claimed invention, a surface stabilizer is introduced to adsorb on the surface of the active agent, thereby preventing agglomeration and promoting stability of a nanoparticulate composition. *See,* for example, page 9, paragraph [0026].

In contrast to the surface stabilizer of the claimed invention, Reiner uses the compounds, e.g., HPMC and polyethylene glycol, to form a lacquer coating on the finished granules rendering them more or less gastro-resistant. Col. 5, lns. 7-12. As such, Reiner does not teach a surface stabilizer adsorbed on the surface of the nimesulide particle because the lacquer comprising HPMC, etc. surrounds the drug layer, not the drug itself. See the illustration above.

The Examiner cites the secondary reference, Ryde, in an attempt to compensate for the deficiencies of Reiner. However, the Examiner fails to articulate a valid reasons why one skilled in the art would modify Reiner in view of Ryde.

(2) Lack of a Reason to Modify Reiner

The Examiner appears to suggest that a person having ordinary skill in the art would have modified Reiner's chewing gum tablet in view of Ryde's teaching that a nanoparticulate active agent composition exhibits dramatic redispersion of the active agent nanoparticles. Nevertheless, one skilled in the art would not have had any reason to improve the redispersibility of that active agent contained within a chewing gum dosage form.

Further to this point, Reiner discusses the advantages of a chewing gum dosage form, e.g., the gum can mask the bitter taste of the drug contained within the gum. *See* Reiner, column 1. If active agent nanoparticles with superior redispersibility were used in Reiner's chewing gum, then the drug would leach from the gum dosage form and quickly redisperse in a patient's mouth. The patient would then be exposed to the bitter taste of the drug, which is exactly what Reiner tries to avoid. See col. 1, lns. 18-22 of Reiner.

Accordingly, the teachings of Reiner expressly contradict the Examiner's supplied reason to modify Reiner in view of Ryde. The Examiner has failed to establish a *prima facie* case of obviousness

B. Reiner, Ryde and Liversidge

Claims 1, 10-13 and 15-26 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Reiner and Ryde in view of U.S. Patent No. 5,552,160 to Liversidge et al. ("Liversidge"). Applicants respectfully traverse the rejection.

C. Reiner, Ryde, Singh and Bosch

Claims 1 and 16-26 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Reiner and Ryde in view of Singh *et al., Analytical Profiles of Drug Substances and Excipients* 28: 197-249, 2001 ("Singh") and in view of U.S. Patent No. 5,510,118 to Bosch et al. ("Bosch"). Applicants respectfully traverse the rejection.

D. Reiner, Ryde, Singh and Merck

Claims 1, 36-38 and 40 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Reiner and Ryde in view of Singh and in view of the Merck Index 12th ed., Merck & Co., 1996, codeine, p416-417 ("Merck"). Applicants respectfully traverse the rejection.

E. Reiner, Ryde and Buhl

Claims 1 and 44 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Reiner and Ryde in view of U.S. Patent No. 5,776,563 to Buhl et al. ("Buhl"). Applicants respectfully traverse the rejection.

All these rejections in headings B-E above rely on Reiner and Ryde, the teachings of which are discussed *supra*. Liversidge is cited for its alleged teaching of pharmacokinetic profiles, e.g., T_{max}, C_{max} and AUC. Singh is cited for the alleged teaching of pharmacokinetic properties, anti-inflammatory and analgesic properties, as well as bioavailability of nimesulide. Bosch is cited for the alleged teaching of modifying bioavailability. Merck simply shows that codeine has analgesic properties. Because these additional references do not remedy the deficiencies of Reiner and Ryde, the rejections under 35 U.S.C. §103(a) should be withdrawn.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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